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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/800,031	03/15/2004	Tara Lynn Bielski	086016-0034	6868

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EXAMINER	
BARHAM, BETHANY P	
ART UNIT	PAPER NUMBER
1615	

MAIL DATE	DELIVERY MODE
11/09/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/800,031	BIELSKI ET AL.	
	Examiner	Art Unit	
	BETHANY BARHAM	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-66* is/are pending in the application.

4a) Of the above claim(s) *61-65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-60 and 66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Summary

Receipt of Applicant's Response filed on 09/24/10 is acknowledged. Claims 1-66 are pending, 61-65 remain withdrawn. Claims 1-60 and 66 are rejected.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/24/10 has been entered.

FINALITY

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

MAINTAINED REJECTIONS

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-60 and 66 is rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,772,473 ('473) in view of US 2003/0180359 ('359) or US 4,792,452 ('452) and US 5,415,871 (‘871).

The instant claims are drawn to an orally administrable formulation for administering nitrofurantoin to a patient in need thereof which comprises: a first component being a controlled release form and a second component being an immediate release form, wherein (a) said first component comprises nitrofurantoin monohydrate, sodium alginate, alginic acid and hypromellose; (b) said second component comprises macrocrystalline nitrofurantoin; and (c) said formulation provides

a therapeutically effective combination of said nitrofurantoin monohydrate and said macrocrystalline nitrofurantoin.

- '473 teaches all the limitations of the instant claims except the first component controlled release excipients. '473 teaches a combination sustained/rapid release pharmaceutical capsule for oral administration of nitrofurantoin comprising a first particulate of nitrofurantoin and sustained release excipients (ie PVP and carboxyvinyl polymer) and a second particulate comprising macrocrystalline nitrofurantoin (abstract, col.5, lines 35-39 and col. 8, lines 18-27). The first particulate comprising nitrofurantoin is nitrofurantoin monohydrate (examples, col. 10, lines 45 and 57-67) (according to the limitations of claim 1).
- '473 teaches that the components are "particulate mixtures" such as powders, granules, etc (col. 3, lines 46-47) and that in the sustained release mixture (first particulate) are uniformly mixed (col. 6, lines 22-26) and that the components can be layered or enclosed in smaller units within the capsule shell containing the entire dosage form (abstract, col. 4, lines 1-19) (meeting the limitations of claims 2, 4-10, 41, 43-52, and 54-60).
- '473 teaches first particulate comprising nitrofurantoin is nitrofurantoin monohydrate (examples, col. 10, lines 45 and 57-67) in amounts of 150-161.4 mg and also generally 50-1000 mg, preferably 100-400, more preferably 150-250mg per capsule (col.6, lines 18-51) (meeting the limitations of claims 11-13). '473 teaches the second particulate comprising macrocrystalline nitrofurantoin is amounts of 10-200 mg, preferably 25-100 mg (col. 6, lines 6-8) (meeting the

limitations of claims 14-16) and thus the ratios of the drugs overlap with those instant claimed in claims 30, 33, 37 and 40).

- '473 teaches the sustained release polymers in amount of 5-86% and 4-40%, etc (col. 7, lines 5-7 and col. 8, lines 29-30) (meeting the limitations of claims 17-26, 30 and 37).
- '473 teaches diluents, fillers, coloring agents, etc (col. 8, lines 48-col. 9, lines 6) and coating the dosage (col. 9, lines 28-39) and about 5% of colorants such as zinc stearate (Examples) (meeting the limitations of claims 28-29, 31-32, 36, 38-39 and 66).
- Stearic acid, talc, lactose, sucrose, etc are all taught as excipients (col. 8, lines 48-col. 9, lines 6) (meeting the limitations of claims 34-35).

'473 does not teach a tablet (instant claims 3, 42, and 53), exact percentages instant claimed, or the sustained release polymers of the first component of alginic acid, sodium alginate and hydroxypropylmethylcellulose (instant claims 1 and 27), but does teach a first particulate comprising nitrofurantoin monohydrate and sustained release polymers/excipients and overlapping percentages.

- '359 teaches multi-layer dosage forms including caplets, tablets, etc [0020] (instant claims 3, 42, and 53). '359 also teaches that controlled release polymers/excipients useful in the active layer include PVP, HPMC (ie hypromellose), carboxyvinylpolymers, alginic acid and derivatives such as sodium alginate [0038]. '359 teaches specifically preferred polymeric substances

for the active layer include a combination of one or more of a) and b), where a) includes HPMC and b) includes alginic acid, sodium alginate [0041] (meeting the limitations of instant claims 1 and 27).

- '452 teaches a controlled release formulation comprising a pharmaceutical and polymers of alginic acid such as sodium alginate and HPMC (abstract, col. 1, lines 11, col. 3, lines 15-60 and Examples). '452 teaches that mixtures of the same or different alginic acid derivatives can be used (col. 3, lines 28-30) (meeting the limitations of instant claims 1 and 27). While '871 teaches that polymer having sustained release properties include sodium alginate or alginic acid and HPMC (col. 4, lines 13-20) and that the can be formulated into any solid dosage such as a gelatin capsule, tablet, etc (col. 6, lines 29-34) (instant claims 3, 42, and 53).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine '473 in view of '359 or '452 and '871. A skilled artisan would know how to substitute the sustained release polymers and/or tablet form of '359 or '452 and '871 for the polymers and/or capsule in the product of '473 with predictable results. Such a substitution of one sustained release polymer for another sustained release polymer is within the purview of the skilled artisan and would yield predictable results.

Furthermore, adjusting the percent of a compound in the formulation is simple optimization and known to a skilled pharmacologist. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454,456, 105 USPQ

233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969).

Response to Arguments

Applicant's arguments with respect to claims 1-60 and 66 have been considered but are not persuasive. Applicant's argue that '473 teaches "the specific excipients polyvinylpyrrolidone and carboxyvinylpolymer are necessary" and "one of ordinary skill in the art would not have substituted the "necessary" (absolutely needed) controlled release excipients taught in the '473 patent with the instantly claimed controlled release excipients" (response page 10, 1st full paragraph). The Examiner respectfully points out that '473 is not relied upon alone but in combination with '359 or '452 and '871 and '473 is only relied upon for its teaching of an sustained release/rapid release oral dosage form comprising a first layer of nitrofurantoin monohydrate and sustained release substituents and a second layer of macrocrystalline nitrofurantoin, and not for its

teaching of the instant claimed sustained release excipients (abstract, col. 4, lines 43-55; col. 10, lines 57-60). '473 in its full disclosure teaches that PVP and carboxyvinylpolymer "are substituents known to be used in sustained release pharmaceutical dosage unit forms" (col. 1, lines 54-56) and that according to the prior art '359 or '452 and '871 other known sustained/controlled release excipients besides PVP and carboxyvinylpolymer include a specifically and preferably a combination of HPMC, sodium alginate and alginic acid (see art citations above). Simple substitution by one of ordinary skill in the art of the sustained release excipients of '473 for other specific sustained release excipients of '359 or '452 and '871 would yield predictable results (see MPEP 2141). Further the Examiner respectfully points out HPMC, alginic acid and sodium alginate are preferred according to '359 or '452 and '871 over the disclosed PVP and carboxyvinylpolymers of '359 and '472 and as such it would be obvious to substitute the preferred excipients of '359 or '452 and '871 into the composition of '473 with predictable results. What Applicants mere arguments have not demonstrated is that such a substitution is unpredictable or that the instant claimed sustained release excipients provide an unexpected result over other unclaimed sustained release excipients via factual evidence, side-by-side comparison, etc. Absent a showing of unexpected results, mere argument by counsel is not persuasive (see MPEP 716.01).

Applicant further argues that "'473 is the only prior art that expressly discloses the active agent nitrofurantoin" and that one of ordinary skill in the art "would not have modified prior art directed specifically to the active agent at issue based on prior art

specifying other actives." The Examiner agrees with Applicant that '473 is relied upon for the teaching of nitrofurantoin, but does not agree that one of ordinary skill in the art who is not an automaton would not know how to substitute known sustained release excipients for other known sustained release excipients. '473 teaches nitrofurantoin and sustained release excipients and in combination with the prior art '359 or '452 and '871 sustained release excipients for dosage forms containing active agents are known preferably to include a combination of HPMC, sodium alginate and alginic acid and as such the rejection of record is maintain and is obvious over the instant claims. Applicant has not shown that nitrofurantoin in the sustained release excipients instant claimed behaves any differently than nitrofurantoin in other known sustained release excipients.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bethany Barham whose telephone number is (571)272-6175. The examiner can normally be reached on M-F, 8:30 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bethany Barham/
Examiner, Art Unit 1615

/S. TRAN/
Primary Examiner, Art Unit 1615